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DICKSTEIN SHAPIRO LLP
1825 EYE STREET NW
Washington, DC 20006-5403

| EXAMINER | |
|---|---|
| GIBBS, TERRA C | |

| ART UNIT | PAPER NUMBER |
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| 1635 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/607,974 | SERRERO, GINETTE | |
| | Examiner | Art Unit | |
| | Terra C. Gibbs | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *8/15/07, 5/11/07, and 1/8/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *28-37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) *40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-37, and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is a response to Applicant's Amendment filed August 15, 2007, Applicant's Election filed May 11, 2007, and Applicant's Amendment and Remarks filed January 8, 2007.

Claims 30 and 40 have been amended. Claim 38 has been canceled.

Claims 28-37, 39, and 40 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Response to Amendment*

Applicant's Amendment filed August 15, 2007 to comply with the requirements of 37 CRF 1.121 is acknowledged. It is noted that the instant application meets the requirements of 37 CFR 1.121(c).

### *Election/Restrictions*

Applicant's election without traverse of Group I, claim 39, drawn to a method of inhibiting the expression of PC Cell Derived Growth Factor protein in cell comprising ministering a PC Cell Derived Growth Factor antisense oligonucleotide comprising SEQ ID NO:14 wherein said oligonucleotide inhibits the expression of PC Cell Derived Growth Factor protein in the reply filed on May 11, 2007 is acknowledged.

Claim 40 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 11, 2007.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 28-37 and 39 have been examined on the merits.

### *Double Patenting*

In the previous Office Action mailed August 15, 2006, claims 28-37 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-7 and 10 of U.S. Patent No. 6,670,183 ('183). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed August 15, 2006.

### *Response to Arguments*

In response to this rejection, Applicants request that this rejection be held in abeyance until the claims are otherwise in a condition for allowance. This request has been considered and it is noted that that this rejection will be held in abeyance until the claims are otherwise in condition for allowance.

### *Claim Rejections - 35 USC § 112*

In the previous Office Action mailed August 15, 2006, claim 34 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention since the term "GP88" is not clearly defined. **This rejection is withdrawn** in view of Applicant's Amendment filed January 8, 2007. Specifically, the Examiner is withdrawing this rejection in view of Applicant's Amendment to the claims to recite the full name of the growth factor.

In the previous Office Action mailed August 15, 2006, claims 28-38 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the growth of a tumor cell or a method of inhibiting the protein expression of 88kDa glycoprotein growth factor (GP88) in a cell, comprising the subcutaneous injection of a GP88 antisense oligonucleotide targeted to SEQ ID NO:16, using primer pairs SEQ ID NO:12 and SEQ ID NO:14, wherein said antisense inhibits the growth of the tumor cell or inhibits the protein expression of GP88, does not reasonably provide enablement for a method of inhibiting the growth of a tumor cell or a method of inhibiting the protein expression of GP88 in a cell, comprising any route of administration of any antisense targeted to GP88, wherein said antisense inhibits the growth of the tumor cell or inhibits the protein expression of GP88. **This rejection is moot** against claim 38 in view of Applicant's Amendment filed January 8, 2007 to cancel this claim. **This rejection is maintained** against claims 28-37 for the reasons of record set forth in the previous Office Action mailed August 15, 2006. It is noted that this rejection is also applied to claim 39.

***Response to Arguments***

In response to this rejection, Applicants argue that in view of the guidance in the specification, the presence of working examples, the state of the prior art, the relative skill of those in the art, and the breadth of the claims, undue experimentation would not be required to practice the claimed invention. Specifically, and for example, Applicants argue that it would not require undue experimentation to determine which cells to target because the claims themselves recite that tumor cells and cells expressing PC Cell Derived Growth Factor protein are the cells to be targeted by the antisense oligonucleotides of the invention. Applicants contend that those of ordinary skill in the art are readily able to identify tumor cells by a variety of methods.

Applicant's argument and contention have been fully considered, but are not found persuasive because while the claims themselves recite that tumor cells and cells expressing PC Cell Derived Growth Factor protein are the cells to be targeted by the antisense oligonucleotides of the invention, the issue is that this recitation does not lend any information towards determining those antisense oligonucleotides which are targeted to PC Cell Derived Growth Factor that carry out the functionality of the instant claims. By way of example, the specification has provided only one antisense oligonucleotide that carries out the *in vivo* functionality of the instant claims. In view of the many discussions regarding the unpredictability of using antisense oligonucleotides in a whole animal, said discussions made of record in the previous Office Actions mailed August 15, 2006 and February 3, 2006, one of ordinary skill in the art would have to perform undue experimentation to practice the invention over the scope

claimed. For further explanation regarding the unpredictability of using antisense oligonucleotides in a whole animal, see the discussions of Branch, A.D.(1998), Jen et al. (2000), Agrawal et al. (2000), and Patil et al. (The AAPS Journal, 2005 Vol. 7, pages E62-E77)) found in the previous Office Actions mailed August 15, 2006 and February 3, 2006.

Applicants next argue that it would not require undue experimentation to practice the invention as claimed since Applicant has provided ample working examples in a well-accepted animal model demonstrating the administration of antisense molecules *in vivo* and the resulting inhibition of tumor cell growth as evidenced by tumor shrinkage. Applicants contend that determining particular dosages, routes of administration, and stability is a matter of routine experimentation and incidental to the claimed invention.

Applicant's argument and contention have been fully considered, but are not found persuasive. The Examiner agrees that Applicant has provided a working example of a method of inhibiting the growth of a tumor cell or a method of inhibiting the protein expression of PC Cell Derived Growth Factor in a cell, comprising the subcutaneous injection of a PC Cell Derived Growth Factor antisense oligonucleotide targeted to SEQ ID NO:16, using primer pairs SEQ ID NO:12 and SEQ ID NO:14, wherein said antisense inhibits the growth of the tumor cell or inhibits the protein expression of PC Cell Derived Growth Factor. However, in view of the unpredictability in the art, this one example does not support the full breadth of the claims drawn to a method of inhibiting the protein expression of PC Cell Derived Growth Factor in a cell, comprising *any* route of injection of *any* PC Cell Derived Growth Factor antisense oligonucleotide targeted to

SEQ ID NO:16. Particularly in view of the discussions regarding the unpredictability of using antisense oligonucleotides provided in the previous Office Actions mailed August 15, 2006 and February 3, 2006, one of ordinary skill in the art would have to perform undue experimentation to practice the invention over the scope claimed (see the discussions of Branch, A.D.(1998), Jen et al. (2000), Agrawal et al. (2000), and Patil et al. (The AAPS Journal, 2005 Vol. 7, pages E62-E77)). For example, due to the scope of the claims, one of skill in the art would be required to undertake extensive trial and error experimentation with a large number of subjects and controls, to determine those antisense targeted to a PC Cell Derived Growth Factor that can be delivered to a mammalian subject such that the growth of a tumor is inhibited. Furthermore, due to the scope of the claims, one of skill in the art would be required to further undertake extensive trial and error experimentation with a large number of subjects and controls, to determine how to deliver those antisense targeted to a PC Cell Derived Growth Factor to a mammalian subject such that the growth of a tumor is inhibited. Due to the extensive trial and error experimentation needed in a large number of subjects and controls, this experimentation would not be a matter of routine experimentation and would be considered undue.

Applicant's next argue that the articles cited by the Examiner in the previous Office Actions show that antisense is a viable technology, particularly where a target for the antisense is identified, as is the case here.

This argument has been fully considered, but is not found persuasive. Applicant is reminded that the instant claims have been afforded priority to May 23, 1997. A

person skilled in the art would recognize that as far back as 1997, antisense gene therapy was in its infancy and was highly unpredictable. It is clear from Branch, A.D.(1998), Jen et al. (2000), and Agrawal et al. (2000), that the state of the art of antisense is unpredictable and those highly skilled in the art are working towards making the art of antisense therapy more predictable but have many obstacles to overcome. Therefore while one skilled in the art, at the time the invention was made, may have viewed antisense as a "viable technology", the technology was then, and is still today "unpredictable" nonetheless and requires undue trial and error experimentation when used in a whole animal to inhibit gene expression or inhibit growth of a tumor in an animal.

Applicants also argue that Applicant provides additional guidance in the specification that would enable one skilled in the art, at the time of the invention was made, to make and use the invention without undue experimentation. For example, Applicants argue that the specification provides guidance for determining suitable PC Cell Derived Growth Factor antisense oligonucleotides and the specification provides guidance for a variety of delivery methods. Applicants point the Examiner to the specification at paragraphs [0113]-[0116] and paragraph [0017], respectively.

This argument has been fully considered, but is not found persuasive because while the specification provides a working example for the subcutaneous injection of a GP88 antisense targeted to SEQ ID NO:16, using primer pairs SEQ ID NO:12 and SEQ ID NO:14, said example being demonstrated to carry out the functionality of the instant claims, the specification teaches other suitable PC Cell Derived Growth Factor

antisense oligonucleotides and other modes of delivery that are all prophetic in nature. Thus, although the specification prophetically considers and discloses general methodologies of using the claimed antisense oligonucleotide *in vivo*, such a disclosure would not be considered enabling since the state of antisense-mediated gene inhibition is highly unpredictable as discussed in the previous Office Actions mailed August 15, 2006 and February 3, 2006.

In sum, in view of the evidence of record, the *Wands* factors have been weighed and favor undue experimentation. Thus, given the broad claims in an art whose nature is identified as unpredictable, the state of the prior art, the lack of guidance in the specification, the breadth of the claims and the quantity of experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention commensurate in scope with these claims.

***Claim Rejections - 35 USC § 112***

In the previous Office Action mailed August 15, 2006, claims 28-37 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. **This rejection is withdrawn** in view of Applicant's Amendment filed January 8, 2007. Specifically, the Examiner is withdrawing this rejection in view of Application Amendment to the claims to recite specific sequence identifiers.

In the previous Office Action mailed August 15, 2006, claims 28-37, 30, 33, and 36 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the

written description requirement. **This rejection is withdrawn** in view of Applicant's Amendment filed January 8, 2007. Specifically, the Examiner is withdrawing this rejection in view of Application Amendment to the claims to recite "about 15-20 nucleotides" and "wherein the proliferation of the tumor cell is inhibited by 80%". It is noted that these limitations are supported by the instant specification at page 35, paragraph [00116] and page 67, paragraph [00197], respectively.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

tcg
October 27, 2007

/Sean McGarry/
Primary Examiner
AU 1635